

64 32. Bacteria of claim 31, wherein said overexpressed aspartate kinase is resistant to inhibition by lysine and/or threonine.

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## II. REMARKS

### PRELIMINARY REMARKS

This response is timely filed as it is accompanied by a petition for an extension of time to file in the first month and a requisite fee.

The applicants wish to thank the examiner for the courtesy shown the undersigned in a telephonic interview conducted during early February 2003. The topic centered on specific amendments to the claims that may place the application in condition for allowance. In view of these discussions, should the examiner, after consideration of the present response and amendment, find further issues with the claims, the examiner is respectfully requested to contact (prior to issuances of an Advisory Action) the undersigned to further discuss these issues.

Support for the foregoing amendment to claims is found throughout the specification and claims as originally filed. For example, support for use of the language "increasing the copy number" found in claims 1 and 3 may be found at page 6, lines 15-19 and page 7, lines 26 *et seq.* The increased copy number may be achieved with plasmids (see examples of present specification) or by chromosomal integration (see Reinscheid *et al.* and L Barre *et al.*, both cited in the specification at page 8, lines 15 and 16). No new matter is believed to have been introduced herein by the foregoing amendment.

The applicants request entry of the foregoing amendment as the applicants believe that the amendment places the application in a condition for allowance or in the alternative places the application in better form for appeal.

On page 2 at section 1 of the official action, the examiner objected to claims 1, 3, 27, 28, and 30-32 for the allegedly inconsistent use of the language "over-expressed" versus "overexpressed." By the foregoing amendment, the claims consistently use the term "overexpressed." Therefore, the applicants request the withdrawal of the rejection.

At section 2 of the official action, the examiner objected to claims 22 and 23 for use of the term "SEQ ID No:" versus "SEQ ID NO:." By the foregoing amendment, the claims 22 and 23 use the term "SEQ ID NO:." Therefore, the applicants request the withdrawal of the rejection.

The examiner also objected to claim 30 with respect to the term “lyseE.” The applicants have corrected this minor error and therefore request withdrawal of the rejection.

#### PATENTABILITY REMARKS

##### Rejection Based Upon 35 U.S.C. §, Second Paragraph

The examiner rejected claim 3 alleging a lack of antecedent basis with respect to the recitation, “the lysE gene.” In response, the applicants submit that this rejection is moot in view of the foregoing amendment to claim 3. Specifically, claim 3 now recites “ a lysE gene.”

The examiner rejected claims 1, 3, 27, 28, and 30-32 for the alleged indefiniteness of the language “over-expressed” or “overexpressed.” The applicants submit that by inclusion of the language “wild type” into the aforementioned claims, such language further defines the scope of the claims and lends definiteness to the language “overexpressed.” Further, the applicants have defined the overexpression as a level above that produce using wild type *corynebacterium glutamicum*.

At section 6 of the official action, the examiner rejected claim 28 for use of the language “said over-expressed aspartate kinase.” The applicants submit that this rejection is also moot. The term “over-expressed” has been removed from the claim.

At sections 7 and 8 of the official action the examiner rejected claim 29 for alleged lackantecedent basis for the lanaguage “the aecD...gene.” The examiner also rejected claim 29 for alleged indefiniteness with respect to the location of the dapA gene. By the foregoing amendment, the applicants amended claim 29 to correct the antecedent basis issue and have refined the defined location of the dapA gene. Therefore, the applicants submit that this rejection is now moot.

In view of the foregoing, the applicants submit that, as amended herein, the claims are neither vague nor indefinite and thereby request that the rejection of the claims under 35 U.S.C. §112, second paragraph be withdrawn.

##### Rejection Based Upon 35 U.S.C. §112, First Paragraph

The examiner rejected claims 1, 3, 27, 28, and 30-32. under 35 U.S.C. §112, first paragraph as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey that the inventors were in possession of the claimed

invention at the time of filing. It is the examiner's position that the "specification fails to adequately described the structures of a genus *C. glutamicum* pyc, lysC, or lysE genes that are overexpressed and a genus of *C. glutamicum* lysC genes overexpressing an aspartate kinase that is resistant to feedback inhibition by lysine and/or threonine.

The examiner admits that the aforementioned genes are well known in the prior art. Taking this in conjunction with the teachings of the specification (how and when to overexpress, -see, for example, above for support on increasing the number of copies of genes) as well as the foregoing amendment to the claims (on how to overexpress the pyc gene), the applicants submit that the claims are neither vague nor indefinite.

At section 10 of the official action, the examiner rejected claims 1, 3, 27, 28, and 30-32 as allegedly being broader than the enabling disclosure. The applicants traverse and submit that as amended herein, the claims are fully enabled by the specification. Specifically, overexpression of the pyc gene is achieved through increasing the copy number of said pyc gene.

In view of the foregoing, the applicants request the withdrawal of the rejection of the claims based upon 35 U.S.C. §112, first paragraph. requesting clarification from the examiner in the aforementioned telephonic interview, the applicants are of the understanding that

Rejection Based Upon 35 U.S.C. §103(a)

The examiner rejected claims 30 and 31 under 35 U.S.C. §103(a) as being unpatentable over DE 19831609 in view of EP 0435132, DE 19548222, and EP 0854189. The examiner alleged that it would have been obvious to one of skill in the art to combine the teachings of a *C. glutamicum* with an expression vector for co-expression of pyc and dapA and/or lysC genes as methods of co-expressing genes in *C. glutamicum* for increased yields of an amino acid are well known in the art.

The examiner rejected claims 3 and 16 as being unpatentable over DE 19831609 in view of EP 0435132 and EP 0854189, in further view of DE 195548222. The examiner alleged that it would have been obvious to combine the teachings of the foregoing documents for a *C. glutamicum* with an expression vector for co-expression of the aforementioned genes.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success.

Finally, the prior art reference (or references when combined) must teach or suggest all of the claim limitations.

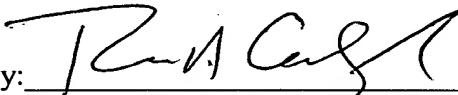
The applicants respectfully submit that the cited documents neither alone nor in combination teach or suggest the simultaneous enhancement of either the *pyc* and *dapA* and *lysE* or *pyc* and *dapA* and *lysC* and *lysE*, via use of the *dapA* promoter selected from the group consisting of: the *dapA* promoter comprising the MC20 mutation as set forth in SEQ ID NO:5 and the *dapA* promoter comprising the MA20 mutation as set forth in SEQ ID NO:6. The applicants submit that the examiner has failed to establish a *prima facie* of obviousness. Therefore, the applicants respectfully request that the rejection of the claims based upon 35 U.S.C. §103(a) be withdrawn.

#### CONCLUSION

In view of the foregoing the claims are now believed to be in form for allowance, and such action is hereby solicited. If any point remains in issue which the examiner feels may be best resolved through a personal or telephone interview, please contact the undersigned at the telephone number listed below.

Respectfully submitted,

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Enclosure: Appendix

APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

The claims are amended as follows:

1. (Twice Amended) L-Lysine-producing bacteria of the species *Corynebacterium glutamicum* comprising an [over-expressed] overexpressed wild type pyc gene of *Corynebacterium glutamicum* encoding pyruvate carboxylase and an [over-expressed] overexpressed wild type dapA gene of *Corynebacterium glutamicum* encoding dihydrodipicolinate synthase, wherein over-expression of said pyc gene is achieved by increasing the copy number of said pyc gene wherein [over-expression] overexpression of said dapA gene is achieved by using a dapA promotor selected from the group consisting of: the dapA promotor comprising the MC20 mutation as set forth in SEQ ID NO:5 and the dapA promotor comprising the MA20 mutation as set forth in SEQ ID NO:6 and whereby said overexpression of said wild type pyc gene of Corynebacterium glutamicum or said wild type dapA gene of Corynebacterium glutamicum gives a pyruvate carboxylase activity or dihydrodipicolinate synthase activity above the level of a wild type Corynebacterium glutamicum.

3. (Twice Amended) Bacteria of claim 1, in which [the] a lysE gene of *Corynebacterium glutamicum* encoding the lysine export carrier is [over-expressed] overexpressed, wherein overexpression of said LysE gene is achieved by increasing the copy number of LysE genes.

22. (Twice Amended) An isolated DNA comprising the nucleotide sequence shown in [SEQ ID No:] SEQ ID NO: 5.

23. (Twice Amended) An isolated DNA comprising the nucleotide sequence shown in [SEQ ID No:] SEQ ID NO: 6.

28. (Amended) Bacteria of claim 27, wherein said [over-expressed] aspartate kinase is resistant to inhibition and/or threonine.

29. (Amended) Bacteria of claim 1, wherein said dapA gene including a dapA promotor selected from the group consisting of: the dapA promotor comprising the MC20 mutation as set forth in SEQ ID NO:5 and the dapA promotor comprising the MA20 mutation as set forth in SEQ ID NO:6 [is comprised in the] wherein said dapA gene, including said dapA promoter is insterted into a aecD (amino ethyl cysteine degrading) gene of Corynebacterium glutamicum.

30. (Amended) L-Lysine-producing bacteria of the species Corynebacterium glutamicum comprising an [over-expressed] overexpressed wild type pyc gene of Corynebacterium glutamicum encoding pyruvate carboxylase, an [over-expressed] overexpressed wild type dapA gene of Corynebacterium glutamicum encoding dihydrodipicolinate synthase, and an [over-expressed] overexpressed wild type [lyseE] lysE gene of Corynebacterium glutamicum encoding lysine export carrier.

31. (Amended) Bacteria of claim 30 further comprising an [over-expressed] overexpressed lysC gene of Corynebacterium glutamicum encoding aspartate kinase.

32. Bacteria of claim 31, wherein said [over-expressed] overexpressed aspartate kinase is resistant to inhibition by lysine and/or threonine.

End of Appendix